# THE CHROMOSOMES IN HEREDITY.

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In a recent announcement of some results of a critical study of the chromosomes in the various cell-generations of *Brachystola*[1] the author briefly called attention to a possible relation between the phenomena there described and certain conclusions first drawn from observations on plant hydrids by Gregor Mendel in[2] 1865, and recently confirmed by a number of able investigators. Further attention has already been called to the theoretical aspects of the subject in a brief communication by Professor E. B. Wilson.[3] The present paper is devoted to a more detailed discussion of these aspects, the speculative character of which may be justified by the attempt to indicate certain lines of work calculated to test the validity of the conclusions drawn. The general conceptions here advanced were evolved purely from cytological data, before the author had knowledge of the Mendelian principles, and are now presented as the contribution of a cytologist who can make no pretensions to complete familiarity with the results of experimental studies on heredity. As will appear hereafter, they completely satisfy the conditions in typical Mendelian cases, and it seems that many of the known deviations from the Mendelian type may be explained by easily conceivable variations from the normal chromosomic processes.

It has long been admitted that we must look to the organization of the germ-cells for the ultimate determination of hereditary phenomena. Mendel fully appreciated this fact and even instituted special experiments to determine the nature of that organization. From them he drew the brilliant conclusion that, while,

[1] Sutton, Walter S., "On the Morphology of the Chromosome Group in Brachystola magna," BIOL. BULL., IV., 1, 1902.

[2] Mendel, Gregor Johann, "Versuche über Pflanzen-Hybriden," *Verh. naturf. Vers. in Brünn* IV., and in Osterwald's *Klassiker der exakten Wissenschaft*. English translation in *Journ. Roy. Hort. Soc.*, XXVI., 1901. Later reprinted with modifications and corrections in Bateson's "Mendel's Principles of Heredity," Cambridge, 1902, p. 40.

[3] Wilson, E. B., "Mendel's Principles of Heredity and the Maturation of the Germ-Cells," *Science*, XVI., 416.

in the organism, maternal and paternal potentialities are present in the field of each character, *the germ-cells in respect to each character are pure.* Little was then known of the nature of cell-division, and Mendel attempted no comparisons in that direction; but to those who in recent years have revived and extended his results the probability of a relation between cell-organization and cell-division has repeatedly occurred. Bateson[1] clearly states his impression in this regard in the following words: "It is impossible to be presented with the fact that in Mendelian cases the cross-bred produces on an average *equal* numbers of gametes of each kind, that is to say, a symmetrical result, without suspecting that this fact must correspond with some symmetrical figure of distribution of the gametes in the cell divisions by which they are produced."

Nearly a year ago it became apparent to the author that the high degree of organization in the chromosome-group of the germ-cells as shown in *Brachystola* could scarcely be without definite significance in inheritance, for, as shown in the paper[2] already referred to, it had appeared that:

1. The chromosome group of the presynaptic germ-cells is made up of two equivalent chromosome-series, and that strong ground exists for the conclusion that one of these is paternal and the other maternal.

2. The process of synapsis (pseudo-reduction) consists in the union in pairs of the homologous members (*i. e.*, those that correspond in size) of the two series.[3]

3. The first post-synaptic or maturation mitosis is equational and hence results in no chromosomic differentiation.

4. The second post-synaptic division is a reducing division, resulting in the separation of the chromosomes which have conjugated in synapsis, and their relegation to different germ-cells.

5. The chromosomes retain a morphological individuality throughout the various cell-divisions.

[1] Bateson, W., "Mendel's Principles of Heredity," Cambridge, 1902, p. 30.

[2] Sutton, W. S., *loc. cit.*

[3] The conclusion that synapsis involves a union of paternal and maternal chromosomes in pairs was first reached by Montgomery in 1901.

Montgomery, T. H., Jr., "A Study of the Chromosomes of the Germ-Cells of Metazoa," *Trans. Amer. Phil. Soc.*, XX.

It is well known that in the eggs of many forms the maternal and paternal chromosome groups remain distinctly independent of each other for a considerable number of cleavage-mitoses, and with this fact in mind the author was at first inclined to conclude that in the reducing divisions all the maternal chromosomes must pass to one pole and all the paternal ones to the other, and that the germ-cells are thus divided into two categories which might be described as maternal and paternal respectively. But this conception, which is identical with that recently brought forward by Cannon,[1] was soon seen to be at variance with many well-known facts of breeding; thus:

1. If the germ-cells of hybrids are of pure descent, no amount of cross-breeding could accomplish more than the condition of a first-cross.

2. If any animal or plant has but two categories of germ-cells, there can be only four different combinations in the offspring of a single pair.

3. If either maternal or paternal chromosomes are entirely excluded from every ripe germ-cell, an individual cannot receive chromosomes (qualities) from more than one ancestor in each generation of each of the parental lines of descent, *e. g.*, could not inherit chromosomes (qualities) from both paternal or both maternal grandparents.

Moved by these considerations a more careful study was made of the whole division-process, including the positions of the chromosomes in the nucleus before division, the origin and formation of the spindle, the relative positions of the chromosomes and the diverging centrosomes, and the point of attachment of the spindle fibers to the chromosomes. The results gave no evidence in favor of parental purity of the gametic chromatin as a whole. On the contrary, many points were discovered which strongly indicate[2] that the position of the bivalent chromosomes

[1] Cannon, W. A., "A Cytological Basis for the Mendelian Laws," *Bull. Torrey Botanical Club*, 29, 1902.

[2] Absolute proof is impossible in a pure-bred form on account of the impossibility of distinguishing between maternal and paternal members of any synaptic pair. If, however, such hybrids as those obtained by Moenkhaus (Moenkhaus, W. J., "Early Development in Certain Hybrid Species," Report of Second Meeting of Naturalists at Chicago, *Science*, XIII., 323), with fishes can be reared to sexual maturity absolute proof of this point may be expected. This observer was able in the early cells

in the equatorial plate of the reducing division is purely a matter of chance — that is, that any chromosome pair may lie with maternal or paternal chromatid indifferently toward either pole irrespective of the positions of other pairs — and hence that a large number of different combinations of maternal and paternal chromosomes are possible in the mature germ-products of an individual. To illustrate this, we may consider a form having eight chromosomes in the somatic and presynaptic germ-cells and consequently four in the ripe germ-products. The germ-cell series of the species in general may be designated by the letters A, B, C, D, and any cleavage nucleus may be considered as containing chromosomes *A*, *B*, *C*, *D* from the father and *a*, *b*, *c*, *d*, from the mother. Synapsis being the union of homologues would result in the formation of the bivalent chromosomes *Aa*, *Bb*, *Cc*, *Dd*, which would again be resolved into their components by the reducing division. Each of the ripe germ-cells arising from the reduction divisions must receive one member from each of the synaptic pairs, but there are sixteen possible combinations of maternal and paternal chromosomes that will form a complete series, to wit : *a*, *B*, *C*, *D* ; *A*, *b*, *C*, *D* ; *A*, *B*, *c*, *D* ; *A*, *B*, *C*, *d* ; *a*, *b*, *C*, *D* ; *a*, *B*, *c*, *D* ; *a*, *B*, *C*, *d* ; *a*, *b*, *c*, *d* ; and their conjugates *A*, *b*, *c*, *d* ; *a*, *B*, *c*, *d* ; *a*, *b*, *C*, *d* ; *a*, *b*, *c*, *D* ; *A*, *B*, *c*, *d* ; *A*, *b*, *C*, *d* ; *A*, *b*, *c*, *D* ; *A*, *B*, *C*, *D*. Hence instead of two kinds of gametes an organism with four chromosomes in its reduced series may give rise to 16 different kinds ; and the offspring of two unrelated individuals may present 16 × 16 or 256 combinations, instead of the four to which it would be limited by a hypothesis of parental purity of gametes. Few organisms, moreover, have so few as 8 chromosomes, and since each additional pair doubles the number of possible combinations in the germ-products[1] and quadruples that of the zygotes it is plain that in the ordinary form having from 24 to 36 chromosomes, the possibilities are immense. The table below shows the number of possible com-

of certain fish hybrids to distinguish the maternal from the paternal chromosomes by differences in form, and if the same can be done in the maturation-divisions the question of the distribution of chromosomes in reduction becomes a very simple matter of observation.

[1] The number of possible combinations in the germ-products of a single individual of any species is represented by the simple formula $2^n$ in which $n$ represents the number of chromosomes in the reduced series.

binations in forms having from 2 to 36 chromosomes in the presynaptic cells.

| Chromosomes. | | Combinations in Gametes. | Combinations in Zygotes. |
|---|---|---|---|
| Somatic Series. | Reduced Series. | | |
| 2 | 1 | 2 | 4 |
| 4 | 2 | 4 | 16 |
| 6 | 3 | 8 | 64 |
| 8 | 4 | 16 | 256 |
| 10 | 5 | 32 | 1,024 |
| 12 | 6 | 64 | 4,096 |
| 14 | 7 | 128 | 16,384 |
| 16 | 8 | 256 | 65,536 |
| 18 | 9 | 512 | 262,144 |
| 20 | 10 | 1,024 | 1,048,576 |
| 22 | 11 | 2,048 | 4,194,304 |
| 24 | 12 | 4,096 | 16,777,216 |
| 26 | 13 | 8,192 | 67,108,864 |
| 28 | 14 | 16,384 | 268,435,456 |
| 30 | 15 | 32,768 | 1,073,741,824 |
| 32 | 16 | 65,536 | 4,294,967,296 |
| 34 | 17 | 131,072 | 17,179,869,184 |
| 36 | 18 | 262,144 | 68,719,476,736 |

Thus if Bardeleben's estimate of sixteen chromosomes for man (the lowest estimate that has been made) be correct, each individual is capable of producing 256 different kinds of germ-products with reference to their chromosome combinations, and the numbers of combinations possible in the offspring of a single pair is $256 \times 256$ or 65,536; while *Toxopneustes*, with 36 chromosomes, has a possibility of 262,144 and 68,719,476,736 different combinations in the gametes of a single individual and the zygotes of a pair respectively. It is this possibility of so great a number of combinations of maternal and paternal chromosomes in the gametes which serves to bring the chromosome-theory into final relation with the known facts of heredity; for Mendel himself followed out the actual combinations of two and three distinctive characters and found them to be inherited independently of one another and to present a great variety of combinations in the second generation.

The constant size-differences observed in the chromosomes of *Brachystola* early led me to the suspicion, which, however, a study of spermatogenesis alone could not confirm, that the individual chromosomes of the reduced series play different *rôles* in development. The confirmation of this surmise appeared later

in the results obtained by Boveri[1] in a study of larvæ actually lacking in certain chromosomes of the normal series, which seem to leave no alternative to the conclusion that the chromosomes differ qualitatively and as individuals represent distinct potentialities. Accepting this conclusion we should be able to find an exact correspondence between the behavior in inheritance of any chromosome and that of the characters associated with it in the organism.

In regard to the characters, Mendel found that, if a hybrid produced by crossing two individuals differing in a particular character be self-fertilized, the offspring, in most cases, conform to a perfectly definite rule as regards the differential character. Representing the character as seen in one of the original parents by the letter A and that of the other by a, then all the offspring arising by self-fertilization of the hybrid are represented from the standpoint of the given character by the formula AA : 2Aa : aa.—that is, one fourth receive only the character of one of the original pure-bred parents, one fourth only that of the other; while one half the number receive the characters of both original parents and hence present the condition of the hybrid from which they sprang.

We have not heretofore possessed graphic formulæ to express the combinations of chromosomes in similar breeding experiments, but it is clear from the data already given that such formulæ may now be constructed. The reduced chromosome series in *Brachystola* is made up of eleven members, no two of which are exactly of the same size. These I distinguished in my previous paper by the letters A, B, C, . . . K. In the unreduced series there are twenty-two elements[2] which can be seen to make up two series like that of the mature germ-cells, and hence may be designated as A, B, C . . . K + A, B, C . . . K. Synapsis results in the union of homologues and the production of a single series of double-elements thus : AA, BB, CC . . . KK, and the reducing division affects the separation of these pairs so that one member of each passes to each of the resulting germ-products.

[1] Boveri, Th., "Ueber Mehrpolige Mitosen als Mittel zur Analyse des Zellkerns," *Verh. d. Phys.-Med. Ges. zu Würzburg*, N. F., Bd. XXXV., 1902. It appears from a personal letter that Boveri had noted the correspondence between chromosomic behavior as deducible from his experiments and the results on plant hybrids—as indicated also in footnote 1, *l. c.*, p. 81.

[2] Disregarding the accessory chromosome which takes no part in synapsis.

There is reason to believe that the division-products of a given chromosome in *Brachystola* maintain in their respective series the same size relation as did the parent element; and this, taken together with the evidence that the various chromosomes of the series represent distinctive potentialities, make it probable that a given size-relation is characteristic of the physical basis of a definite set of characters. But each chromosome of any reduced series in the species has a homologue in any other series, and from the above consideration it should follow that these homologues cover the same field in development. If this be the case chromosome *A* from the father and its homologue, chromosome *a*, from the mother in the presynaptic cells of the offspring may be regarded as the physical bases of the antagonistic unit-characters A and a of father and mother respectively. In synapsis, copulation of the homologues gives rise to the bivalent chromosome *Aa*, which as is indicated above would, in the reducing division, be separated into the components *A* and *a*. These would in all cases pass to different germ-products and hence in a monœcious form we should have four sorts of gametes,

$$A\,♂ \qquad a\,♂$$
$$A\,♀ \qquad a\,♀$$

which would yield four combinations,

$$A\,♂ + A\,♀ = AA$$
$$A\,♂ + a\,♀ = Aa$$
$$a\,♂ + A\,♀ = aA$$
$$a\,♂ + a\,♀ = aa$$

Since the second and third of these are alike the result would be expressed by the formula $AA : 2Aa : aa$ which is the same as that given for any character in a Mendelian case. *Thus the phenomena of germ-cell division and of heredity are seen to have the same essential features, viz., purity of units (chromosomes, characters) and the independent transmission of the same;* while as a corollary, it follows in each case that each of the two antagonistic units (chromosomes, characters) is contained by exactly half the gametes produced.

The observations which deal with characters have been made

chiefly upon hybrids, while the cytological data are the result of study of a pure-bred form; but the correlation of the two is justified by the observation of Cannon [1] that the maturation mitoses of fertile hybrids are normal. This being the case it is necessary to conclude, as Cannon has already pointed out, that the course of variations in hybrids either is a result of normal maturation processes or is entirely independent of the nature of those divisions. If we conclude from the evidence already given that the double basis of hybrid characters is to be found in the pairs of homologous chromosomes of the presynaptic germ-cells, then we must also conclude that in pure-bred forms likewise, the paired arrangement of the chromosomes indicates a dual basis for each character. In a hypothetical species breeding absolutely true, therefore, all the chromosomes or subdivisions of chromosomes representing any given character would have to be exactly alike, since the combination of any two of them would produce a uniform result. As a matter of fact, however, specific characters are not found to be constant quantities but vary within certain limits; and many of the variations are known to be inheritable. Hence it seems highly probable that homologous chromatin-entities are not usually of strictly uniform constitution, but present minor variations corresponding to the various expressions of the character they represent. In other words, it is probable that specific differences and individual variations are alike traceable to a common source, which is a difference in the constitution of homologous chromatin-entities. Slight differences in homologues would mean corresponding, slight variations in the character concerned — a correspondence which is actually seen in cases of inbreeding, where variation is well known to be minimized and where obviously in the case of many of the chromosome pairs both members must be derived from the same chromosome of a recent common ancestor and hence be practically identical.

In the various forms of parthenogenesis we meet the closest kind of inbreeding and a brief consideration of the variability to be expected in each, from the standpoint of the chromosome theory, may serve as a guide to such research as will test the

[1] Cannon, W. A., *loc. cit.*

validity of the latter. The simplest form, of which chemical parthenogenesis in sea-urchins is an examble, is that in which the organism has only a single chromosome series, to be represented by *A*, *B*, *C*, *D*... *N*. Thus far no recognized cases of this type have been reared to sexual maturity, but it is to be expected that no reducing division will be found in the maturation of such forms, and that their parthenogenetic offspring will exactly resemble the immediate parent.

In cases of natural parthenogenesis which are accompanied by the reëntrance of the second polar body and its fusion with the egg-nucleus (or its failure to form) there must be a double chromosome series; but we may distinguish two classes according as the reducing process is accomplished in the first or the second maturation division.[1] If reduction is accomplished in the first division, one half the chromosomes of the oögonia are thrown out and lost in the first polar body. The second division, being equational, would result in a polar body which would be the exact duplicate of the egg-nucleus as far as chromosomes are concerned and which accordingly, by its reëntrance would add nothing new to the egg-series. The series after fusion would, therefore, be represented by the letters *A*, *B*, *C*, *D*... *N* + *A*, *B*, *C*, *D*... *N*. If such a type of parthenogenesis were to follow sexual reproduction, the first generation of offspring might be expected to differ materially from the parent by reason of the casting out, in the first polar body, of chromosomes representing certain dominant characters, and the consequent appearance in the offspring of the corresponding recessives. Subsequent parthenogenetic generations, however, would in each case be endowed with a chromosome series exactly similar to that of the immediate parent and accordingly might be expected to show the same characters.

In case the second division of a parthenogenetic egg were the reducing division, the reëntrance or suppression of the second polar body would accomplish the restoration of the oögonial chromosome-series. In this case the first parthenogenetic gen-

[1] Either must be regarded as possible in cases where we have no definite knowledge since it is regularly described as the second in the Orthoptera (McClung, Sutton and Copepoda (Rückert, Häcker) while in the Hemiptera-Heteroptera it is believed to be the first (Paulmier, Montgomery).

eration might be expected to duplicate the characters of the parent (if environmental conditions remained unchanged) and little or no variability would be expected as long as parthenogenesis persisted.

In relation to these problems there is great need of a simultaneous study of the germ-cell divisions and the variation of periodically parthenogenetic forms.

We have seen reason, in the foregoing considerations, to believe that there is a definite relation between chromosomes and allelomorphs[1] or unit characters but we have not before inquired whether an entire chromosome or only a part of one is to be regarded as the basis of a single allelomorph. The answer must unquestionably be in favor of the latter possibility, for otherwise the number of distinct characters possessed by an individual could not exceed the number of chromosomes in the germ-products; which is undoubtedly contrary to fact. We must, therefore, assume that some chromosomes at least are related to a number of different allelomorphs. If then, the chromosomes permanently retain their individuality, it follows that all the allelomorphs represented by any one chromosome must be inherited together. On the other hand, it is not necessary to assume that all must be apparent in the organism, for here the question of dominance enters and it is not yet known that dominance is a function of an entire chromosome. It is conceivable that the chromosome may be divisible into smaller entities (somewhat as Weismann assumes), which represent the allelomorphs and may be dominant or recessive independently. In this way the same chromosome might at one time represent both dominant and recessive allelomorphs.

Such a conception infinitely increases the number of possible combinations of characters *as actually seen* in the individuals and unfortunately at the same time increases the difficulty of determining what characters are inherited together, since usually recessive chromatin entities (allelomorphs?) constantly associated in the same chromosome with usually dominant ones would evade detection for generations and then becoming dominant might appear as reversions in a very confusing manner.

[1] Bateson's term.

In their experiments on *Matthiola*, Bateson and Saunders[1] mention two cases of correlated qualities which may be explained by the association of their physical bases in the same chromosome. "In certain combinations there was close correlation between (*a*) green color of seed and hoariness, (*b*) brown color of seed and grabrousness. In other combinations such correlation was entirely wanting." Such results may be due to the association in the same chromosomes of the physical bases of the two characters. When close correlation was observed, both may be supposed to have dominated their homologues; when correlation was wanting, one may have been dominant and the other recessive. In the next paragraph to that quoted is the statement: "The rule that plants with flowers either purple or claret arose from green seeds was universal." Here may be a case of constant dominance of two associated chromatin-entities.

Dominance is not a conception which grows out of purely cytological consideration. Cytology merely shows us the presence in a cell of two chromosomes, either of which is capable of producing some expression of a given character, and it is left to experiment in each case to show what the effect of this combined action will be. The experiment[2] has shown that any one of the three theoretical possibilities may be realized, viz: (1) One or the other may dominate and obscure its homologue. (2) The result may be a compromise in which the effect of each chromosome is to be recognized. (3) The combined action of the two may result in an entirely new cast of character. In cases belonging to the first category, the visible quality (allelomorph, chromatin-entity) was described by Mendel as dominant and the other as recessive, and the experiments of Bateson and Saunders and others, as well as those of Mendel, have shown that in many cases a dominant character tends to remain dominant during successive generations if the environment is not materially changed. Nevertheless, some experiments cited by Bateson[2] go to show that dominance may be variable or defective. Furthermore, it is not only conceivable, but highly probable that in most, if not all

[1] Bateson and Saunders, Experimental Studies in the Physiology of Heredity. Reports to the Evolution Committee, I. London, 1902, p. 81, paragraphs 11 and 12.

[2] *Cf.* Bateson and Saunders, *loc. cit.*

cases, there are many different expressions of each character (*i. e.*, many different allelomorphs as suggested by Bateson [3] in regard to human stature), which on various combinations would necessarily exhibit relative dominance. The experiments with peas show an almost constant dominance of certain allelomorphs, such as round over wrinkled in seeds, and of yellow over green in cotyledons; but it is worthy of note that here, as in most Mendelian experiments, only two antagonistic characters have been used. Investigations on varieties, in general similar, but exhibiting different expressions of some particular character, will certainly yield instructive results. Bateson's observations on crosses between single-, rose- and pea-combed fowls, represent a simple form of such a case and may be expected on completion to add much to our knowlege of the nature of dominance.

In addition to the many examples brought forward by Bateson in support of the Mendelian principle he cites three types of cases which are to be regarded as non-Mendelian. These are:

1. The ordinary blended inheritance of continuous variation.
2. Cases in which the form resulting from the first cross breeds true.
3. The "false hybrids" of Millardet.

1. *Blended Inheritance.* — In treating of this class Bateson clearly states the possibility that the case may be one entirely "apart from those to which Mendel's principles apply," but goes on to show how it may possibly be brought into relation with true Mendelian cases. He says in part: "It must be recognized that in, for example, the stature of a civilized race of man, a typically continuous character, there must certainly be on any hypothesis more than one pair of possible allelomorphs. There may be many such pairs, but we have no certainty that the number of such pairs and consequently of the different kinds of gametes are altogether *unlimited*, even in regard to stature. If there were even so few as, say, four or five pairs of possible allelomorphs, the various homo- and heterozygous combinations might, on seriation, give so near an approach to a continuous curve that the purity of the elements would be unsuspected, and their detection practically impossible." This hypothesis, which presents no difficulties from the point of view of the chromosome theory, is

sufficient in the present state of our knowledge to bring many cases of apparently continuous variation into definite relation with strictly Mendelian cases; but, on the other hand, it seems probable, as already noted (p. 221), that the individual variation in many characters now thought to be strictly Mendelian may prove to be due to the existence in the species of many variations of what may be regarded as the type allelomorphs, accompanying similar variations of the homologous chromatin entities representing those types.

2. *First Crosses that Breed True.* — It is obvious that in the germ-cells of true-breeding hybrids[1] there can be no qualitative reduction. In the normal process synapsis must be accounted for by the assumption of an affinity existing between maternal and paternal homologues, and conversely reduction is the disappearance of that affinity or its neutralization by some greater force. Now in *Hieracium* the characters of the hybrid are frequently intermediate between those of the two parents, showing that both allelomorphs (or chromatin-entities) are at work, but on self fertilization there is no resolution of allelomorphs (reduction division). On the contrary, all the germ-cells are equivalent, as shown by the fact that all combinations produce similar offspring which in turn are similar to the parent. The suggestion made by Bateson in another connection, that "if one allelomorph were alone produced by the male and the other by the female we should have a species consisting *only* of heterozygotes," which would come true as long as bred together, at first sight seems logically applicable to these cases. For such an idea, however, we can find no cytological justification, since if any reduction occurs both chromosomes occur in both male and female germ-cells in equal numbers; and further, the evidence is in favor of a great variety of combinations of maternal and paternal chromosomes in the germ-cells so that the exact chromosome group of a hybrid parent could hardly be duplicated except by fusion of the very pair of cells separated by the reducing division. A more plausible explanation from the cytological standpoint is that the union of the chromosomes in synapsis is so firm that no reduction can take place, *i. e.*, that in each case, a paternal and

[1] *Cf.* Mendel's experiments on *Hieracium*.

a maternal chromosome fuse permanently to form a new chromosome which subsequently divides only equationally. The result must be germ-cells which are identical with one another and with those of the parents, and hence self-fertilization would produce offspring practically without variation. If this explanation be the correct one the process is distinctly pathological and hence it is not surprising that such cases, as noted by Bateson, should often present "a considerable degree of sterility."

3. *The "False Hybrids" of Millardet.* — Millardet, de Vries and Bateson have all described experiments in which the offspring resulting from a cross between dissimilar individuals showed the character of one parent only, those of the other parent being shown by further experiment to be lost permanently. The obvious cytological explanation of such a phenomenon is hinted at by Bateson in the words "Such phenomena may perhaps be regarded as fulfilling the conception of Strasburger and Boveri, that fertilization may consist of two distinct operations, the stimulus to development and the union of characters in the zygote."[1] Division of the egg without fusion of the pronuclei in a well-known phenomenon having been observed in eggs treated with chloral (Hertwig brothers) or ether (Wilson) and may be supposed to occur under certain unusual conditions in nature. In the experiments mentioned, however, both pronuclei continue to divide separately, while for a cytological explanation of the occurrence of "false hybrids" it is necessary to conceive not only the failure of the nuclei to copulate but the entire disappearance of one of them. Such a case would be comparable to that of chemically induced parthenogenesis or to the fertilization of enucleate egg-fragments, according as the nucleus remaining was maternal or paternal. Speculation in this connection, however, is unprofitable excepting so far as it may serve as a guide to research. A careful study of the fertilization of such cases as Millardet's strawberries, de Vries's *Oenothera* and Bateson's *Matthiola* crosses will no doubt be productive of immediate and positive results.

*Mosaics.*— A fourth class of non-Mendelian cases, the "mosaics" or "piebalds" constitute a group in relation to which, as I believe, only negative evidence is to be expected

[1] Bateson and Saunders, *loc. cit.*, p. 154.

from direct cytological study. A good example of the class is the "mosaic" fruit of *Datura* obtained by Bateson and Saunders, which, although in general exhibiting the thornless recessive condition, showed in exceptional cases a thorny patch. Of this case Bateson says: "Unless this is an original sport on the part of the individual, such a phenomenon may be taken as indicating that the germ-cells may also have been mosaic." I must confess my failure to comprehend just what is here meant by mosaic germ-cells. I have attempted to show that in all probability the germ-cells are normally a mosaic of maternal and paternal chromosomes, but very evidently this is not Bateson's meaning.

From the standpoint of the chromosome theory I would suggest a possible explanation of the conditions as follows: We have already assumed that the somatic chromosome group, having a similar number of members to that of the cleavage nucleus and derived from it by equation divisions, is made up in the same way of pairs of homologous chromosomes. Every somatic cell, by this conception, must contain a double basis in the field of each character it is capable of expressing. In strictly Mendelian cases one of the homologues is uniformly dominant throughout the parts of the organism in which the character is exhibited. As already noted, however, it is unlikely that all the descendants of a dominant chromatin entity will be dominant. This is shown by the experiment of de Vries with sugar beets, which are normally biennial but always produce a small percentage of annual plants or "runners," which latter are regarded as recessives. The percentage of these runners may be increased by rearing the plants under unfavorable conditions and this is taken as evidence that the recessive allelomorphs may become dominant under such conditions.[1]

If each cell contains maternal and paternal potentialities in regard to each character, and if dominance is not a common function of one of these, there is nothing to show why as a result of some disturbing factor one body of chromatin may not be called into activity in one group of cells and its homologue in another. This would produce just the sort of a mosaic which Bateson and

[1] *Cf.* Bateson and Saunders, pp. 135, 136.

Saunders found in *Datura* or as Tchermak's pied yellow and green peas obtained by crossing the *Telephone* pea with yellow varieties. Correns describes the condition as *pœcilodynamous* and his conception of the causes of the phenomenon as I understand it is parallel with that which I have outlined above. The logical possibility suggested by Bateson[1] that the recessive islands in such cases as the mosaic pea may be due to recessive allelomorphs in the paired state does not accord with the theory of a chromosomic basis for those allelomorphs, since the chromosome groups, both of cells showing the recessive character and of neighboring cells showing the dominant one, are derived, so far as we know, by longitudinal or equation division from the chromosomes of the same original cleavage nucleus and hence must be alike.

The application of the theory here suggested may be put to test by an experiment in which hybrids of dissimilar true-breeding parentage are crossed and a third generation of "quarter-bloods" produced. Mosaics occurring in such an organism, if this theory be correct, would show one character resembling that of one of the maternal grandparents and one resembling that of one of the original pure-breds of the paternal side. If both characters of the mosaic should be clearly paternal or maternal the theory as outlined is proven inadequate, since one of each pair of chromosomes, and hence the corresponding character-group, is thrown out by the reduction-division in each generation.

In considering the behavior of the two chromosomes forming the basis of any given character, it was noted that in some cases the heterozygote character resulting from the combinations of dissimilar allelomorphs is sometimes totally unlike either of the latter. Thus Mendel found that in crosses between peas respectively 1 and 6 feet in height the offspring ranged from 6 to 7½ feet. In discussing similar cases, Bateson calls attention to the light which would be thrown on the phenomenon if we ventured to assume that the bases of the two allelomorphs concerned are chemical compounds; and he compares the behavior of the allelomorphs to the reaction of sodium and chlorine in the formation

[1] Bateson and Saunders, p. 156.

of salt. The results of chemical analysis show that one of the most characteristic features of chromatin is a large percentage content of highly complex and variable chemical compounds, the nucleo-proteids, and therefore if, as assumed in the theory here advanced, the chromosomes are the bases of definite hereditary characters, the suggestion of Bateson becomes more than a merely interesting comparison.

We have seen reason in the case of the true-breeding hybrids to suspect that the transmission by the hybrid of heterozygote characters may be due to permanant union of the homologous chromosomes. From this it is but a short step to the conclusion that even if, as is normally the case, the chromosomes do not fuse permanently, the very fact of their association in the same liquid medium may allow a possibility of a certain degree of chemical interaction. This must normally be slight, since its effects do not appear to be visible in a single generation; but the slightest of variation as a result of repeated new association, even though it tend in diverse directions, must in time, guided by natural selection, result in an appreciable difference in a definite direction between a chromosome and its direct descendant and hence between the characters associated with them. In this we have a suggestion of a possible cause of individual variation in homologous chromosomes which we have already seen reason to suspect (pp. 221 and 226).

Finally, we may briefly consider certain observations which seem at first sight to preclude the general applicability of the conclusions here brought out. If it be admitted that the phenomenon of character-reduction discovered by Mendel is the expression of chromosome-reduction, it follows that forms which vary according to Mendel's law must present a reducing division. But the vertebrates and flowering plants—the very forms from which most of the Mendelian results have been obtained—have been repeatedly described as not exhibiting a reducing division. Here, therefore, is a discrepancy of which I venture to indicate a possible explanation in the suggestion first made by Fick[1] and more recently by Montgomery.[2] This is to the effect that in

[1] Fick, R., "Mittheilung ueber Eireifung bei Amphibien," *Supp. Anat. Anz.*, XVI.
[2] Montgomery, T. H., Jr., *loc. cit.*

synapsis as it occurs in vertebrates and other forms possessing loop-shaped chromosomes, the union is side by side instead of end-to-end to as in Arthropods. In vertebrates, two parallel longitudinal splits, the forerunners of the two following divisions, appear in the chromosomes of the primary spermatocyte prophases. Both being longitudinal, they have been described as equation divisions, but if it shall be found possible to trace one to the original line of union of the two spermatogonial chromosomes side by side in synapsis, that division must be conceived as a true reduction. A number of observations supporting this view will be brought forward in my forthcoming work on *Brachystola*.

Again, if the normal course of inheritance depends upon the accurate chromatin-division accomplished by mitosis, it would appear that the interjection, into any part of the germ cycle, of the gross processes of amitosis could result only in a radical deviation from that normal course. Such an occurrence has actually been described by Meves, McGregor and others in the primary spermatogonia of amphibians. In these cases, however, it appears that fission of the cell-body does not necessarily follow amitotic division of the nucleus. I would suggest, therefore, the possibility that the process may be of no significance in inheritance, since by the disappearance of the nuclear membranes in preparation for the first mitotic division, the original condition is restored, and the chromosomes may enter the equatorial plate as if no amitotic process had intervened.

There is one observation in connection with the accessory chromosome which deserves mention in any treatment of the chromosomes as agents in heredity. This element always divides longitudinally and hence probably equationally. It fails to divide in the first maturation mitosis, in which the ordinary chromosomes are divided equationally, but passes entire to one of the resulting cells. In the second maturation division, by which the reduction of the ordinary chromosomes is effected, the accessory divides longitudinally.[2]

[1] It is of interest in connection with this question that there occurs regularly in each of the spermatogonial generations in *Brachystola* a condition of the nucleus which suggests amitosis but which in reality is nothing more than the enclosure of the different chromosomes in partially separated vesicles. Cf. Sutton, W. S., "The Spermatogonial Divisions in Brachytola Magna," *Kans. Univ. Quart.*, IX., 2.

[2] The chromosome *x* of *Protenor*, which of all chromosomes in non-orthopteran

My observations in regard to the accessory chromosome lend support to the hypothesis of McClung[1] that of the four spermatozoa arising from a single primary spermatocyte, those two which contain this element enter into the formation of male offspring, while the other two, which receive only ordinary chromosomes take part in the production of females. If this hypothesis be true, then it is plain that in the character of sex the reduction occurs in the first maturation mitosis, since it is this division which separates cells capable of producing only males from those capable of producing only females. Thus we are confronted with the probability that reduction in the field of one character occurs in one of the maturation divisions and that of all the remaining characters in the other division. The significance of such an arrangement, though not easy of perception, is nevertheless great. As regards their chromosome groups, the two cells resulting from each reduction mitosis are conjugates and, therefore, opposites from the standpoint of any individual character. Thus if we consider a hypothetical form having eight chromosomes comprising the paternal series *A*, *B*, *C*, *D* and the maternal series *a*, *b*, *c*, *d*, one of the cells resulting from the reduction division might contain the series *A*, *b*, *c*, *D*, in which case its sister-cell would receive the conjugate series *a*, *B*, *C*, *d*. It is plain that these conjugates, differing from each other in every possible character, represent the most widely different sperms the organism can produce. Now if reduction in the sex-determining chromatin also took place in this division it is apparent that these two diametrically opposite series would enter into individuals of different sexes; but if the sex-reduction is previously accomplished by the asymmetrical distribution of the accessory in the first division, then both the members of each conjugate pair must take part in the production either of males or of females and thus

forms most closely resemble the accessory, is also described by Montgomery (1901) as dividing in the reducing division, and failing to divide in the equation division—a fact which is the more remarkable because in *Protenor*, as in all Hemiptera-Heteroptera thus far described, reduction is accomplished in the *first* maturation division.

[1] McClung, C. E., "The Accessory Chromosome — Sex Determinant?" BIOL. BULL., III., 1 and 2, 1902. "Notes on the Accessory Chromosome," *Anat. Anz.*, XX., pp. 220–226.

all extremes of chromosome combination are provided for within the limits of each sex.

## Postscript.

The interesting and important communication of Guyer[1] on "Hybridism and the Germ-Cell" is received too late for consideration in the body of this paper. This investigator also has applied conclusions from cytological data to the explanation of certain phenomena of heredity, and his comparative observations on the spermatogenesis of fertile and infertile hybrids are an important contribution to the cytological study of the subject. The conclusions drawn are of great interest but, I think, in some cases, open to criticism. In assuming that there is a "segregation of maternal and paternal chromosomes into separate cells, which may be considered 'pure' germ-cells containing qualities of only one species" (p. 19), he repeats the error of Cannon which has already been dealt with in the early part of this paper. No mention is made in the paper of Mendel's law but in considering the inbred pigeon hybrids from which his material was obtained, the author expresses his familiarity with manifestations of the Mendelian principle by the statement that "in the third generation there is generally a return to the original colors of the grandparents." In cases which seem to resemble one grandparent in all particulars it is clear that the conception of pure germ-cells may be strictly applied, but the author was familiar with cases of inbred hybrids which plainly show mixtures. These he is inclined to explain in two ways as follows: (1) "Union of two cells representing each of the two original species would yield an offspring of the mixed type." (2) "Besides through the mixing just indicated, variability may be due also in some cases to the not infrequent inequalities in the division of individual chromosomes, through which varying proportions of the chromatin of each species may appear in certain of the mature germ-cells" (p. 20).

The first of these explanations would accord with the result of Mendelian experiment but for the fact that it is erroneously applied (and without cytological grounds) to *all* the characters or chromosomes instead of to individuals. As for the second

[1] Guyer, M. F., "Hybridism and the Germ-Cell," *Bulletin of the University of Cincinnati*, No. 21, 1902.

passage quoted, there can be little doubt that irregular division of chromosomes would be likely to produce marked variation, but as Guyer himself observes, *these irregularities increase with the degree of infertility*. It seems natural to conclude, therefore, that they are not only pathological but perhaps in part the cause of the infertile condition. Furthermore, on the hypothesis of individuality of chromosomes, which Guyer accepts, the loss of a portion of a chromosome by irregular division would be permanent and the effect of repetitions of the operation upon the descendants of a single chromosome group (which he regards as transmitted as a whole) would be so marked a depletion of chromatic substance as must lead soon to malfunction and ultimately to sterility.

As already noted (p. 216) the first of these two explanations of the causes of variation would allow only four possible combinations of chromosomes in the offspring of a single pair. But we know that except in the case of identical twins, duplicates practically never appear in the offspring of a pair however numerous the progeny. Therefore, whatever the number of the offspring, the variations of all except the few provided for by the four normal chromosome combinations must be accounted for by obviously pathological division processes, which tend strongly in the direction of sterility. But in the report of Bateson and Saunders to the Evolution Committee we find the statement: "We know no Mendelian case in which fertility is impaired" (p. 148). When we reflect that the vast majority of cases studied by these observers were Mendelian and connect this piece of evidence with the testimony of Cannon [1] that the maturation processes of variable cotton-hybrids are either normal or so distinctly abnormal as to entail sterility and with Guyer's own admission that the abnormalities in mitosis increase with the degree of sterility, the balance is strongly against the efficacy of pathological mitoses as factors in normal hybrid variation.

I take pleasure in acknowledging my indebtedness to Professor E. B. Wilson for invaluable counsel in the presentation of a subject offering many difficulties.

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January 25, 1903.

[1] Cannon, W. A., *loc. cit.*